REMARKS

Status of claims:

Claims 1, 5-8, 13-15, 17-34, 36-45 and 48-73 were pending. Claims 5-8, 51-62 and 68-73 were withdrawn as drawn to non-elected subject matter. Claims 2-4, 9-13, 16, 31, 35 and 46-47 are canceled without prejudice or disclaimer. Applicants reserve the right to prosecute the canceled subject matter in a continuation or divisional application. Claims 1, 14, 15, 17-30, 32-34, 36-45, 48-50 and 63-67 are presently under consideration.

Claims 1, 18, 32, 37 and 45 are amended herein to clarify that the water-solubilizing moiety is selected from the Markush group consisting of an aminopolycarboxylate, ethylenediaminetetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA), triethylenetetraminehexaacetic acid (TTHA), benzyl-DTPA, 1,4,7,10-tetraazacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA), benzyl-DOTA, 1,4,7-triazacyclononane- N,N',N"-triacetic acid (NOTA), benzyl-NOTA, a polyethylene glycol (PEG), and N,N'-dialkyl substituted piperazine. The amendment is supported at least in original claims 13, 14 and 31 and the published Specification at paragraphs [0033], [0038], [0071], [0072], [0076], [0080], [0083] and [0084] and Examples 3, 7, 8 and 9.

Claim 14 is amended to avoid dependence from a canceled claim and to eliminate recitation of PEG.

Applicant submits that no new matter is added by the amendment.

Rejection of claims under 35 U.S.C. 112, 1st paragraph

Claims 1, 15, 17, 18-30, 32-34, 36-45, 48-50 and 63-67 are rejected under 35 U.S.C. 112, 1st paragraph for lack of written description support. The Action asserts that there is insufficient written description support for the genus of "water-solubilizing moiety". Although Applicant traverses the rejection, the independent claims are amended herein to recite that the water-solubilizing moiety is selected from the Markush group consisting of an aminopolycarboxylate, ethylenediaminetetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA),

triethylenetetraminehexaacetic acid (TTHA), benzyl-DTPA, 1,4,7,10-tetraazacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA), benzyl-DOTA, 1,4,7-triazacyclononane- N,N',N"-triacetic acid (NOTA), benzyl-NOTA, a polyethylene glycol (PEG), and N,N'-dialkyl substituted piperazine. Applicant notes that the language of the amended independent claims essentially tracks that of previously dependent claims 13, 14 and 31, and that those claims were not rejected under 35 U.S.C. 112, 1st paragraph for lack of written description support. Applicant submits that the claims as amended find ample written description support in the application as filed.

Rejection of claims under 35 U.S.C. 103

Claims 1, 13-14, 17-24, 27-31, 33-34, 36-43 and 48-50 were rejected under 35 U.S.C. 103 as unpatentable over Chari et al. (WO 01/24763, hereafter "Chari") in view of Hsel et al. (U.S. 7,122,636, hereafter "Hsel").

Claims 25 and 44 were rejected under 35 U.S.C. 103 as unpatentable over Chari et al. in view of Hsel et al. and further in view of Newton et al. (Blood 2001, 97:528-35, hereafter "Newton").

Claims 63-67 were rejected under 35 U.S.C. 103 as unpatentable over Chari et al. in view of Hsel et al. and further in view of Govindan et al. (U.S. 7,238,785, hereafter "Govindan").

Applicant initially notes that Govindan is only 102(e)/103 prior art to the instant application and shares a common inventor with the instant application. Applicant's representative states that Govindan (U.S. Patent 7,238,785) and the subject matter claimed in the instant application were commonly owned, or subject to an obligation of assignment to the same person (Immunomedics, Inc.) at the time the claimed invention was made. Therefore Govindan is disqualified as 102(e)/103 prior art under 35 U.S.C. 103(c).

Applicant further notes that claims 15, 26, 32 and 45 were not rejected over the prior art.

Therefore, since the rejection under 35 U.S.C. 112, 1st paragraph is overcome, at least claims 15, 26, 32, 45 and 63-67 should be considered allowable.

The distinction between the cited prior art references and the instant claimed subject matter is discussed below.

Chari et al. (WO 01/24763 A2)

Claim 1 recites that the chemotherapeutic moiety is attached to the linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester moiety formed from the α-carboxylic acid of an amino acid. It is a requirement of the claim limitation that the ester bond is cleavable by intracellular esterases.

Claim 1 further recites that the ester bond is between the chemotherapeutic moiety and an α-amino acid. An α-amino acid would be understood by one skilled in the art to refer to the 20 naturally occurring L-amino acids. This is significant because intracellular esterases have evolved to cleave ester bonds formed from naturally occurring amino acids.

In contrast, Chari teaches that the ester bond is between the antimitotic drug and carboxylic acid derivatives that *are not naturally occurring amino acids*. The amino acids used by Chari are N-methylated versions [Chari, pg. 6-7] that are not cleavable by intracellular esterases. Thus, despite the phrase that "suitable linking groups [include] esterase labile groups" on page 6, Chari uses only the "preferred disulfide groups and thioether groups" and discloses only esters of N-methylated versions of amino acids [Chari, pg. 6-7]. As stated by the Action, "the WO publication teaches...that the linking group is part of the chemical moiety having a peptide such as N-methyl-cysteine or N-methyl-alanine, covalently bound at the C-terminus to an anti-mitotic agent, such as a maytansinoid derivative, via an ester linkage." *The relevance of this is that intracellular esterases will not recognize an unnatural or an N-alkylated amino acid as a substrate to act on.* Thus, Chari fails to teach or disclose the element of attaching a chemotherapeutic moiety to a linker via a intracellularly-cleavable moiety that comprises an ester formed from the α-carboxylic acid of an amino acid. In fact, Chari teaches away from the claimed subject matter by leading the skilled artisan to use linkages that are not intracellularly cleavable.

Under MPEP 2143.03, the prior art must be viewed in its entirety, considering not only that section which may have similarity to the claimed invention, but also sections that teach away

from the claimed invention. The disclosure of Chari is fundamentally different from the instant claimed subject matter, in that Chari discloses a combination therapy using an immunoconjugate and, separately, a therapeutic agent. The instant claims recite an antibody linked to a chemotherapeutic agent (via a linker group) to form an immunoconjugate. Thus, Chari's disclosure of a combination therapy in which the chemotherapeutic agent is administered separately from the immunoconjugate teaches away from the instant invention.

Hsel (US patent 7,122,636)

The Action asserts that Hsel teach conjugates formed by antibody fragments attached to nonproteinaceous polymer molecules, such as PEG. The Action does not assert that Hsel teaches or discloses aminopolycarboxylates other than PEG. Claim 14 is amended to eliminate PEG from the list of recited water-soluble moieties.

Hsel also fails to remedy the deficiency of Chari, in that it also contains no disclosure relevant to the incorporation of an intracellularly cleavable ester moiety formed from the α-carboxylic acid of an amino acid. Thus, considering Chari and Hsel together, there is no teaching or disclosure in the cited prior art that would lead the skilled artisan to incorporate intracellularly cleavable ester moiety formed from the α-carboxylic acid of an amino acid in the immunoconjugate of claim 1.

Newton et al (Blood 2001; 97:528-535)

With respect to the reference of Newton, that reference is cited by the Action as merely disclosing, "an immunoconjugate comprising LL2 covalently linked to the ribonuclease, onconase, wherein LL2 is an anti-CD22 monoclonal antibody against B-cell lymphoma." [Action at pg. 8, 3rd paragraph] There is no citation to Newton as disclosing anything relating to "a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on the antibody, and (ii) a water-solubilizing moiety, wherein the chemotherapeutic moiety is attached to the linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α-carboxylic acid of an amino acid," elements of amended claim 1.

Thus, none of the references, either alone or in combination, teach or suggest the limitation of a chemotherapeutic moiety attached to a linker "via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α-carboxylic acid of an amino acid."

Based upon these references an ordinary artisan would have no reasonable expectation of success in reaching the claimed compositions. Therefore, Applicant respectfully submits that claim 1 is not obvious over the cited prior art. Since the other claims all depend from or otherwise contain the limitations of claim 1, along with additional elements, Applicant respectfully submits that none of the pending claims are obvious over the cited prior art.

Conclusion

In conclusion, Applicant respectfully submits that the pending claims as amended are all in condition for allowance and an early decision to that effect is requested.

Respectfully submitted,

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Dated: June _20_, 2008